

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2004/001572

## A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. <sup>7</sup>: C12Q/100, 1/25

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPIDS, MedLine, CA, BIOSIS, Biotechabs: cbl, c-cbl, acetyl coA carboxylase, amp dependent protein kinase, fatty acid level/oxidation, antibody/antisense/ribozyme/RNAi/dominant/negative, insulin/diabetes .

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 2004/055181 A1 (GARVAN INSTITUTE OF MEDICAL RESEARCH) 1 July 2004 Whole document	1-113
P, X	Molero JC et al. c-Cbl-deficient mice have reduced adiposity, higher energy expenditure, and improved peripheral insulin action. J Clin Invest, 2004. 114(9): 1326-33. Whole document.	1-113
A	Farese RV. Function and dysfunction of aPKC isoforms for glucose transport in insulin-sensitive and insulin resistant states. Am J Physiol Endocrinol Metab, 2002. 283: E1-E11.	1-113
A	Vollenweider P. Insulin resistant states and insulin signalling. Clin Chem Lab Med, September 2003. 41(9): 1107-1119.	1-113

☒ Further documents are listed in the continuation of Box C☒ See patent family annex

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search  
23 February 2005Date of mailing of the international search report  
- 1 MAR 2005Name and mailing address of the ISA/AU  
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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Khan AH et al. Insulin regulation of glucose uptake: a complex interplay of cellular pathways. Diabetologia, 2002. 45:1475-83.	1-113
A	Abu-Elheiga L et al. AcetylCoA carboxylase 2 mutant mice are protected against obesity and diabetes induced by high fat/high carbohydrate diets. Proc Natl Acad Sci USA, 2 Sept 2003. 100(18): 10207-212.	1-47
A	Winder WW et al. Activation of AMP-activated protein kinase increases mitochondrial enzymes in skeletal muscle. J Appl Physiol, 2000. 88: 2219-26	48-94
A	Joazeiro CAP et al. The tyrosine kinase negative regulator c-Cbl as a RING-type E2-dependent ubiquitin-protein ligase. Science, 1999. 286: 309-311.	97-113
A	Chiusaroli R et al. Deletion of a gene encoding c-Cbl alters the ability of osteoclasts to migrate, delaying resorption and ossification of cartilage during the development of long bones. Develop Biol, 2003. 261:537-47.	97-113
A	Murphy MA et al. Tissue hyperplasia and enhanced T cell signalling via ZAP-70 in c-Cbl deficient mice. Mol Cell Biol, 1998. 18(8): 4872-82.	97-113
A	Sohn HW et al. Cbl-b negatively regulates B cell antigen receptor signalling in mature B cells through ubiquitination of the tyrosine kinase Syk. J Exp Med, June 2003. 197(11): 1511-24.	97-113
A	Liu J et al. The roles of Cbl-b and c-Cbl in insulin stimulated glucose transport. J Biol Chem 19 September 2003. 278(38): 36754-762.	97-113
A	Griffiths EK et al. Cbl-3 deficient mice exhibit normal epithelial development. Mol Cell Biol, November 2003. 23(21): 7708-18.	97-113
A	Melikova MS, Filatova MM, Kornilova ES. Cbl - a polyfunctional regulator of cellular processes. Tsitologiya, 2003;45(11):1134-48. [Article in Russian] PubMed Abstract 14989153.	97-113

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**Supplemental Box**

(To be used when the space in any of Boxes I to VIII is not sufficient)

**Continuation of Box No: III - Lack of Unity**

The present claims are directed to seven inventions.

- **Invention 1**, defined by claims 1-96 is to methods of identifying compounds that modulate insulin sensitivity comprising administering the compound to a cell tissue or animal having reduced Cbl expression and determining activities of specific enzymes or level of specific metabolites.
- **Invention 2** defined by claims 97-113 is to a method of identifying a therapeutic target for the treatment of aberrant insulin action by reducing Cbl expression or activity, and determining the effect of this on other genes/proteins. Genes or proteins with changed expression or activity are identified as therapeutic targets.
- **Invention 3**, defined by claims 114-115 is to methods of identifying compounds that modulate acetyl coA carboxylase activity by measuring Cbl expression/activity in the presence and absence of the compound.
- **Invention 4**, defined by claims 116-117 is to methods of identifying compounds that modulate AMP dependent kinase activity by measuring Cbl expression/activity in the presence and absence of the compound.
- **Invention 5**, defined by claims 118-121 is to methods of identifying compounds that modulate free fatty acid synthesis or modulate fatty acid oxidation by measuring Cbl expression/activity in the presence and absence of the compound.
- **Invention 6**, defined by claims 122-123 is to methods of identifying compounds that modulate uncoupling protein 3 activity by measuring Cbl expression/activity in the presence and absence of the compound.
- **Invention 7**, defined by claims 116-117 is to methods of identifying compounds that modulate insulin receptor expression by measuring Cbl expression/activity in the presence and absence of the compound.

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**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:  
The ISA found 7 inventions –see Supplemental Box III

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:1-113
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

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**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International application No.  
**PCT/AU2004/001572**

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report	Patent Family Member
WO 2004/055181	AU 2002/953393
Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.	
END OF ANNEX	

BES1 AVAILABLE COPY